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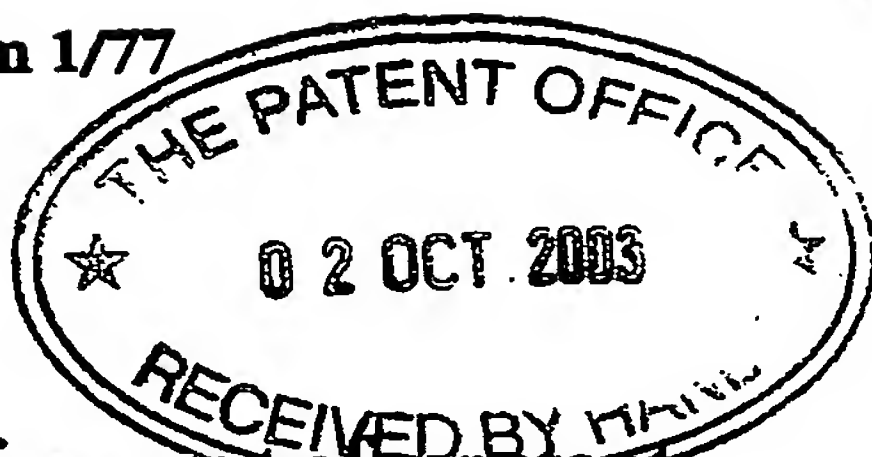
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P017780 0.00-0323090.1

Request for grant of a patent

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The Patent Office

Cardiff Road
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South Wales
NP10 8QQ

1. Your reference

PPD 70252/GB

2. Patent application number

(The Patent Office will fill in this part)

02 OCT 2003

0323090.1

3. Full name, address and postcode of the or of each applicant (*underline all surnames*)

08029555001

Patents ADP number (*if you know it*)

SYNGENTA PARTICIPATIONS AG
Intellectual Property Department
Schwarzwaldallee 215
4058 Basel
SWITZERLAND

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention

NOVEL PROCESS

5. Name of your agent (*if you have one*)

"Address for service" in the United Kingdom to which all correspondence should be sent (*including the postcode*)

Jane Elizabeth SWIFT
Intellectual Property Department
Syngenta Limited
Jealott's Hill International Research Centre
PO Box 3538
Bracknell, Berkshire, RG42 6YA
UNITED KINGDOM

Patents ADP number (*if you know it*)

08148298002

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (*if you know it*) the or each application number

Country

Priority application number
(*if you know it*)

Date of filing
(*day / month / year*)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing
(*day / month / year*)

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (*Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or

b) there is an inventor who is not named as an applicant, or

c) any named applicant is a corporate body.

See note (d))

YES (b)

Patents Form 1/77

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Continuation sheets of this form 03 ✓

Description 01 ✓

Claim(s) 00

Abstract 00

Drawing(s) 00

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10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

Request for preliminary examination and search (Patents Form 9/77)

Request for substantive examination (Patents Form 10/77)

Any other documents (please specify)

11.

I/We request the grant of a patent on the basis of this application.

SYNGENTA PARTICIPATIONS AG
Signature
Authorised Signatory

M A Rudd

Date 02/10/03

12. Name and daytime telephone number of person to contact in the United Kingdom

Margaret Ann RUDD

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Notes

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NOVEL PROCESS

The present invention relates to a novel process for the preparation of 2-(2'-nitro-4'-methylsulphonylbenzoyl)-1,3-cyclohexanedione (mesotrione).

5 The current process for preparing mesotrione requires the reaction of cyclohexanedione with 2-nitro-4-methylsulphonylbenzoylchloride to give the enol ester, followed by a rearrangement process resulting in mesotrione. The reaction is carried out in a suitable solvent in the presence of an organic base and an appropriate catalyst. After formation of the product, the solvents are removed and the pH of the solution increased
10 to approximately 11-12.5 by the addition of sodium hydroxide to give a suspension of the insoluble sodium enolate salt in a mixture of water and organic base. Crystallisation of the mesotrione product is effected by the controlled addition of 10% HCl down to a pH of approximately 2.8. The resulting product is then collected by appropriate means, for example using a centrifuge.

15 However, we have now found that following this process occasionally results in undesirable impurities being present in the final mesotrione product. A further problem with this process is that at a pH of 11-12.5, the organic base is present as the free base and is partially immiscible with the aqueous components of the mixture. It is not possible to separate the organic base from the mixture due to the presence of the solid sodium
20 enolate of mesotrione. Similarly, it is not possible to separate any other organic immiscible solvents from this mixture or to carry out a purification process with solid phase absorbents due to the presence of solids.

Accordingly, one object of the present invention is to provide an improved process for the preparation of mesotrione that results in a purer final product.

25 A second object of the invention is to provide a method of purifying mesotrione (prepared by any method) to result in a purer final product.

Accordingly, the present invention provides a process for the preparation of mesotrione, said process comprising the steps of:

- (i) reaction of cyclohexanedione with 2-nitro-4-
30 methylsulphonylbenzoylchloride in an appropriate solvent and in the presence of an organic base to give the enol ester,
- (ii) rearrangement of the enol ester to give mesotrione,
- (iii) removal of the solvent, and thereafter
- (iv) formation of a soluble enolate salt of mesotrione,
- 35 (v) one or more purification steps, and

- (vi) crystallisation of mesotrione.

In another aspect of the invention, there is provided a process for the purification of mesotrione, said process comprising the steps of:

- 5 (i) formation of a soluble enolate salt of mesotrione,
(ii) one or more purification steps, and
(iii) crystallisation of mesotrione.

The process for the reaction of cyclohexanedione and 2-nitro-4-methylsulphonylbenzoylchloride and the rearrangement reaction may be carried out as described in EP0186117, and which is incorporated herein by reference.

10 The formation of a soluble enolate salt of mesotrione may be carried out by the addition of a suitable second base to the mesotrione-containing solution. Examples of suitable bases include, but are not limited to, potassium hydroxide, ammonium hydroxide, pyridine and triethylamine. Most preferred is potassium hydroxide.

15 The purification process may include one or more purification steps, carried out in any order. Examples of suitable purification steps include, but are not limited to the following:

- 20 1) removal of the organic base (either by a batch or a continuous method) prior to the crystallisation step. This results in improved purification, since any impurities which are soluble in the organic base, but insoluble in the aqueous phase are removed. It is also possible to add additional quantities of the organic base and perform multiple extractions to further improve the purification. Since the organic base can be removed prior to crystallisation, this also minimises the organic load of the mesotrione solution in the next process steps
- 25 2) the addition of an immiscible solvent to the enolate solution. Any impurities soluble in this solvent will then be removed with the removal of the solvent prior to crystallisation. Examples of suitable solvents include, but are not limited to, chlorobenzene, toluene, anisole, 1,2-dichloroethane, n-butyronitrile, iso-butyronitrile, benzonitrile, tetrahydrofuran, o-xylene, mixed xylenes,
- 30 3) treatment of the mesotrione enolate solution with a solid absorbent, for example activated charcoal, silica, alumina, zeolites, etc.

Crystallisation may be carried out by any method known in the art, for example by reducing the pH of the solution by the controlled addition of HCl.

The process of the invention results in a cleaner mesotrione product with less undesirable impurities.

A further advantage of the process of the present invention is that the crystallisation process is from a homogenous mixture, which will result in a more robust
5 crystallisation process and improved operability (e.g. better pH control).

Claims

1. A process for the preparation of mesotrione, said process comprising the steps of:
 - (i) reaction of cyclohexanedione with 2-nitro-4-methylsulphonyl benzoylchloride in an appropriate solvent and in the presence of an organic base to give an enol ester,
 - (ii) rearrangement of the enol ester to give mesotrione,
 - (iii) removal of the solvent, and thereafter
 - (iv) formation of a soluble enolate salt of mesotrione,
 - (v) one or more purification steps, and
 - (vi) crystallisation of mesotrione.
2. A process for the purification of mesotrione, said process comprising the steps of:
 - (i) formation of a soluble enolate salt of mesotrione,
 - (ii) one or more purification steps, and
 - (iii) crystallisation of mesotrione.
3. A process according to any one of claims 1 or 2, wherein the formation of the soluble enolate salt is carried out by addition of a second base to the mesotrione-containing solution.
4. A process according to claim 3, wherein the second base is selected from the group consisting of potassium hydroxide, ammonium hydroxide, pyridine and triethylamine.
5. A process according to claim 4, wherein the second base is potassium hydroxide.
6. A process according to any one of claims 1 or 2, wherein the purification step includes one or more of the following: removal of the organic base; addition of an immiscible solvent to the enolate solution; treatment of the enolate solution with a solid absorbent.